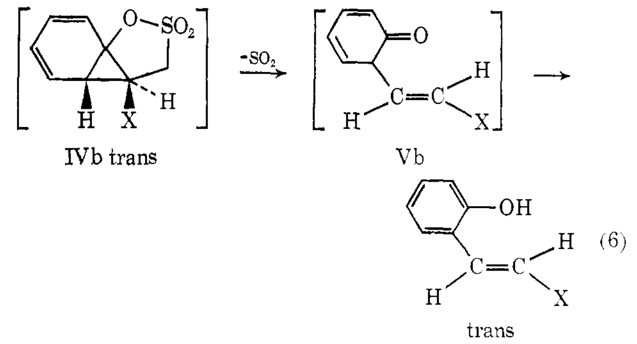
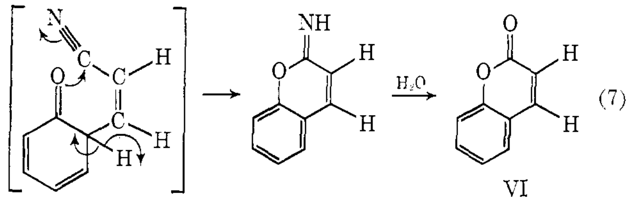
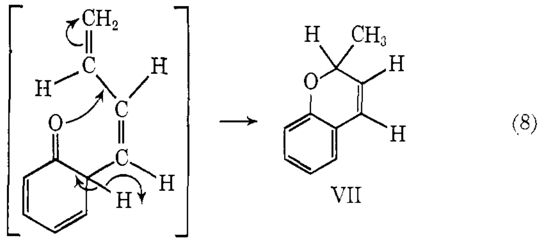

IVb trans Vb trans

in reaction path occurs when "X" in Va is -CN or -CH=CH$_2$; subsequent cyclization yields VI and VII (eq 7 and 8).


VI


VII

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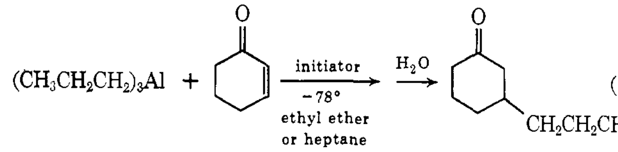
Reaction of Tri-*n*-propylaluminum with α,β-Unsaturated Ketones. Evidence for a Free-Radical Chain Mechanism

Sir:

We wish to report the first unequivocal example of a free-radical chain reaction involving trialkylaluminum compounds. Tri-*n*-propylaluminum reacts readily with α,β-unsaturated ketones in the presence of radical initiators at $-78°$ producing the conjugate addition products exclusively. In the absence of free-radical initiators, no reaction occurs. The reaction is exemplified by the synthesis of 3-*n*-propylcyclohexanone (eq 1).

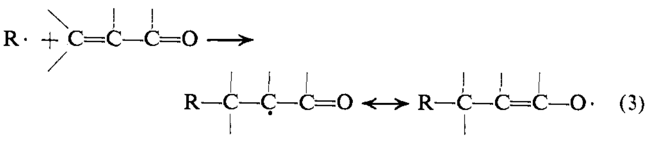


There has been a great deal of interest in recent years focused on the free-radical reactions of organometallic compounds. Excellent reviews on this subject have recently appeared.[1,2] It is known that an S$_H$2 process can occur readily at an aluminum center (eq 2).[3,4] If

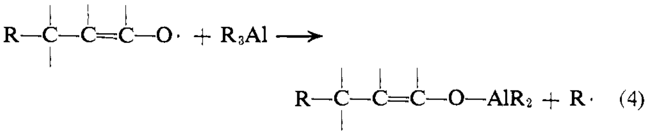
$$R'O\cdot + R_3Al \longrightarrow R'OAlR_2 + R\cdot \qquad (2)$$

the alkyl radical thus produced could be caused to regenerate an alkoxy radical, a chain process would result. This has been demonstrated to be the case for the autoxidation of organoboranes and alkyltin chlorides[5] as well as for the 1,4-addition reactions of organoboranes.[6] It has been postulated that the autoxidation of organoaluminum compounds proceeds *via* a free-radical chain reaction but the evidence is not compelling.[7]

In view of our recent studies on the free-radical reactions of organoboranes, it seemed reasonable to expect that a trialkylaluminum compound would undergo an analogous free-radical chain reaction with an α,β-unsaturated carbonyl compound (eq 3 and 4).[6,8]



$$R\cdot + >C{=}\overset{|}{C}-\overset{|}{C}{=}O \longrightarrow R-\underset{|}{\overset{|}{C}}-\underset{\bullet}{\overset{|}{C}}-\overset{|}{C}{=}O \longleftrightarrow R-\underset{|}{\overset{|}{C}}-\overset{|}{C}{=}\overset{|}{C}-O\cdot \qquad (3)$$



$$R-\underset{|}{\overset{|}{C}}-\overset{|}{C}{=}\overset{|}{C}-O\cdot + R_3Al \longrightarrow R-\underset{|}{\overset{|}{C}}-\overset{|}{C}{=}\overset{|}{C}-O-AlR_2 + R\cdot \qquad (4)$$

Previous attempts to achieve the conjugate addition of trialkylaluminum compounds to α,β-unsaturated systems had been unsuccessful,[9] generally leading to polymerization[10] or 1,2-addition products.[11,12] It appeared likely that the carbonyl addition reaction could be eliminated simply by lowering the reaction temperature to take advantage of the relatively high E_A of this process (approximately 19 kcal/mol).[13]

We have found this to be the case. Tri-*n*-propylaluminum does not react with 2-cyclohexenone at $-78°$ in alkane or ether solvents even after a period of 30 hr.[14] However, in the presence of radicals generated by irradiation, a 75% yield of 3-*n*-propylcyclo-

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[1] K. U. Ingold and B. P. Roberts, "Free Radical Substitution Reactions," Wiley-International, New York, N. Y., 1971.

[2] A. G. Davies and B. P. Roberts, *Accounts Chem. Res.*, **5**, 387 (1972).

[3] A. G. Davies and B. P. Roberts, *J. Organometal. Chem.*, **19**, P17 (1969).

[4] P. J. Krusic and J. L. Kochi, *J. Amer. Chem. Soc.*, **91**, 3942 (1969).

[5] A. G. Davies, T. Maki, and B. P. Roberts, *J. Chem. Soc., Perkin Trans. 2*, 744 (1972).

[6] G. W. Kabalka, H. C. Brown, A. Suzuki, S. Honma, A. Arase, and M. Itoh, *J. Amer. Chem. Soc.*, **92**, 710 (1970).

[7] A. G. Davies and B. P. Roberts, *J. Chem. Soc. B*, 1074 (1968).

[8] H. C. Brown, M. M. Midland, and G. W. Kabalka, *J. Amer. Chem. Soc.*, **93**, 1024 (1971).

[9] (a) Although no successful 1,4-addition reactions of trialkylaluminum reagents have been achieved, H. Gilman and R. Kirby did achieve the 1,4 addition of triphenylaluminum to benzalacetophenone [*J. Amer. Chem. Soc.*, **63**, 2046 (1941)]. (b) A successful 1,4-addition reaction of trialkylaluminum reagents was reported by Y. Kawakami [*J. Macromol. Sci. Chem. A*, **3** (2), 205 (1969)]. Our attempts to reproduce the reported reactions under the conditions described lead to quantitative 1,2 addition of the organoaluminum reagent to the carbonyl group.

[10] T. Tsuruta, R. Fujio, and J. Fumkawa, *Macromol. Chem.*, **80**, 172 (1964).

[11] Y. Baba, *Bull. Chem. Soc. Jap.*, **41**, 928 (1968).

[12] A. R. Lyons and E. Catterall, *J. Organometal. Chem.*, **25**, 351 (1970).

[13] E. C. Ashby, S. Yu, and P. Roling, *J. Org. Chem.*, **37**, 1918 (1972).

[14] Tri-*n*-propylaluminum was added to an equimolar quantity of 2-cyclohexenone in ethyl ether (temperature maintained at $-78°$). After 30 hr, the mixture was hydrolyzed. Glpc analysis indicated quantitative recovery of 2-cyclohexenone. Similar results were obtained utilizing 3-penten-2-one.

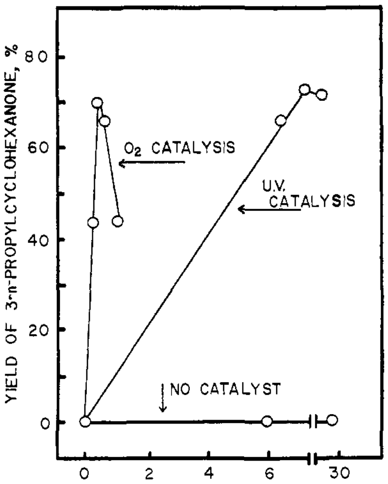

Figure 1. Reaction of tri-*n*-propylaluminum (0.25 *M*) with 2-cyclohexenone (0.25 *M*) in heptane at −78°. The effect of free-radical initiators.

Table I. Photochemically Induced Reaction of Tri-*n*-propylaluminum with Representative α,β-Unsaturated Ketones[a]

Ketone	Product[b]	Bp, °C[c]	Yield, %[d,e]	Time[f]
2-Cyclohexenone	3-*n*-Propylcyclohexanone	211	75 (70)[g]	7 hr
3-Penten-2-one	4-Methyl-2-heptanone	156	60	1 hr
Methyl vinyl ketone	2-Heptanone	152	30[h]	1 min

[a] Reaction conditions: 5 mmol of organoaluminum added to 5 mmol of ketone dissolved in heptane and maintained at −78°. Ultraviolet light shone on the mixture for an indicated period of time. [b] All products were either compared with authentic samples or exhibited analytical and spectral data in accordance with the assigned structures. [c] 745 mm. [d] Yields calculated using starting ketone as limiting reagent. [e] By glpc analysis. [f] Time of reaction at which maximum yield was obtained, in all cases starting materials still present. [g] The value in parentheses refers to an experiment in which oxygen was utilized as the radical initiator. [h] Polymerization occurred.

hexanone (after hydrolysis) is obtained in 7 hr under otherwise identical conditions.[15]

Essentially identical yields are obtained when traces of oxygen[16] are employed as the free-radical initiator except that the maximum yield is attained more quickly. The results of the photochemical and oxygen-induced reactions are shown graphically in Figure 1.

Galvinoxyl, an efficient free-radical scavenger, has been used successfully to inhibit extremely fast free-radical chain reactions of organometallic compounds.[1,17] We have found that the addition of 5 mol % of galvinoxyl effectively stops the otherwise facile photochemically induced reaction of tri-*n*-propylaluminum with 2-cyclohexenone. The results are shown graphically in Figure 2.

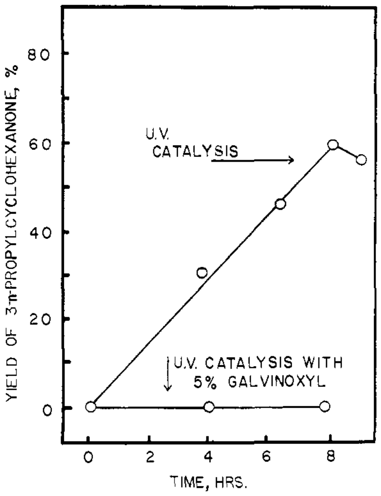

Figure 2. Reaction of tri-*n*-propylaluminum (0.25 *M*) with 2-cyclohexenone (0.25 *M*) in ethyl ether. The effect of added galvinoxyl (in mole %).

The reaction appears to be a general one. Thus, 1,4-addition products are obtained in the reactions of tri-*n*-propylaluminum with a variety of α,β-unsaturated ketones. In all cases, no 1,2-addition products were observed. Furthermore, we have made no effort to maximize yields as of this date. Our results are summarized in Table I. The experimental details are essentially those described earlier.[15]

The discovery that tri-*n*-propylaluminum can be made to participate in such a facile free-radical addition process opens up a major new area for exploration. Such a study is in progress.

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[15] H. C. Brown and G. W. Kabalka, *J. Amer. Chem. Soc.*, **92**, 712 (1970).

[16] Traces of oxygen are most conveniently added to the reaction mixture by simply adding air at a slow rate (~0.1 ml/min) [H. C. Brown and G. W. Kabalka, *J. Amer. Chem. Soc.*, **92**, 714 (1970)].

[17] P. D. Bartlett and T. Funahashi, *J. Amer. Chem. Soc.*, **84**, 2596 (1962).

Carbon-13 Nuclear Magnetic Resonance and Infrared Spectroscopic Studies of ^{13}CO Binding to Rabbit Hemoglobin[1]

Sir:

Recently it has been reported[2] that two ^{13}C resonances of equal intensity, chemical shift separation 2 ppm, can be distinguished for ^{13}CO bound to Fe(II) of the heme units of the α and β chains of rabbit hemoglobin. The chemical shift separation reported for the two ^{13}CO resonances of rabbit hemoglobin is quite large considering that (1) although two ^{13}CO resonances can be distinguished in the spectra of carbonyl hemoglobins of other species (*e.g.*, mouse, dog, and human), not only are there smaller chemical shifts (~0.4 ppm) between the α and β chains but also between the ^{13}CO resonances of carbonyl hemoglobins from different species,[2,3] and (2) the ^{13}CO resonance of

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[1] This work was performed under the auspices of the U. S. Atomic Energy Commission and the U. S. Public Health Service (Grant No. HL-15980).

[2] R. B. Moon and J. H. Richards, *J. Amer. Chem. Soc.*, **94**, 5093 (1972).

[3] N. A. Matwiyoff, P. J. Vergamini, T. S. Needham, R. T. Eakin, C. Barlow, C. T. Gregg, and W. C. Caughey, manuscript in preparation.